IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re application of | ) | |
| Christian E. Schafmeister | ) | |
| Serial No. 10/613,961 | ) | Examiner Rita J. Desai |
| Confirmation No. 9015 | ) | Group Art Unit 1625 |
| Filed July 05, 2003 | ) | Attorney Docket No. 214001-01024-1-1 |
| For BIS(AMINO ACID) | ) | |
| MOLECULAR SCAFFOLDS | ) | |

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Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION OF CHRISTIAN E. SCHAFMEISTER
UNDER 37 C.F.R. 1.132

I, Christian E. Schafmeister, Ph.D., declare and state:

My professional experience is as follows:

1. From August 1983 through August 1990, I was a student at Simon Fraser University Vancouver, British Columbia, Canada, where I received my Bachelor of Science in Chemistry degree.

From August 1990 through August 1991, I worked on software development at the University of California in San Francisco.

From August 1991 through August 1997, I was a Doctoral Student at the University of California at San Francisco, where I received a Doctorate in Biophysics. My area of research was developing a new method for maintaining solubility of membrane proteins using amphipathic peptides and designed, synthesized and characterized a four helix bundle protein.

From August 1997 through May 2000, I was a Postdoctoral Fellow at Harvard University, Boston, Massachusetts. My area of research was the development of a synthetic approach to stabilizing elements of peptide secondary structure.

From January, 2001 until the present time, I have been an Assistant Professor at the University of Pittsburgh, Pittsburgh, Pennsylvania.

2. My current research at the University of Pittsburgh is in the development and study of functional macromolecules constructed from asymmetric molecular building blocks.

3. I am an author of numerous publications in the area of functional macromolecules (see Publication Attachment).

4. I received the following Fellowships:

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| 1997-2000 | Fellow of the Jane Coffin Childs Memorial Fund |
| 1997 | Cancer Research Institute Post-doctoral Fellowship (declined to accept the Jane Coffin Childs Fellowship). |
| 1997 | Canadian Natural Science and Engineering Post-doctoral Fellowship (declined to accept the Jane Coffin Childs Fellowship.) |
| 1991-1997 | Howard Hughes Predoctoral Fellow. |
| 1991 | National Science and Engineering Research Council of Canada Predoctoral fellowship (declined to accept the Howard Hughes Predoctoral Fellowship). |

5. I received the following awards:

1. Research Corporation, Research Innovation Award, 2000-2002
2. Camille and Henry Dreyfus New Faculty Award, 2000-2005
3. Cottrell Scholarship Award, 2004-2009
4. Feynman Prize for Experimental Nanotechnology, 2005

6. I am a named inventor of the captioned application Serial No. 10/613,961 and I have an inventor's understanding of the United States Patent System.

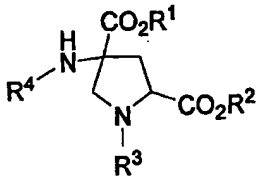
7. I have reviewed the current amendment to the captioned application Serial No. 10/613,961 which is now directed to linked compounds and now contains functional language from the body of the specification.

8. I have read the Examiner's Office action dated February 13, 2006, which rejected the claims 1 and 4-8 as unpatentable over references U.S. 5,473,077 and WO9605828, both of which I have also read.

9. With regard to the Examiner's statements based on the WO reference in scheme II, III and IV on pages 15 and 16, and the newly amended inclusion of linked compounds and functional language now in the claims versus teachings of U.S. 5,473,077 and WO9605828:

10. That, to one skilled in the art, the building blocks that we claim in claims 1,4-8 (Serial No. 10/613,961) have a limited resemblance to the compounds described in WO9605828 (see figure below). However, our building blocks have the one carboxyl group to be a carboxylic acid and the other to be a "weak leaving group", a term that we define but that falls within the definition of a carboxyl protecting group within the definition of a carboxyl protecting group on page 9 of WO9605828. Our building blocks (Serial No. 10/613,961) also have each of the amines on the building block protected with an amino-protecting group.

**GENERAL FORMULA**



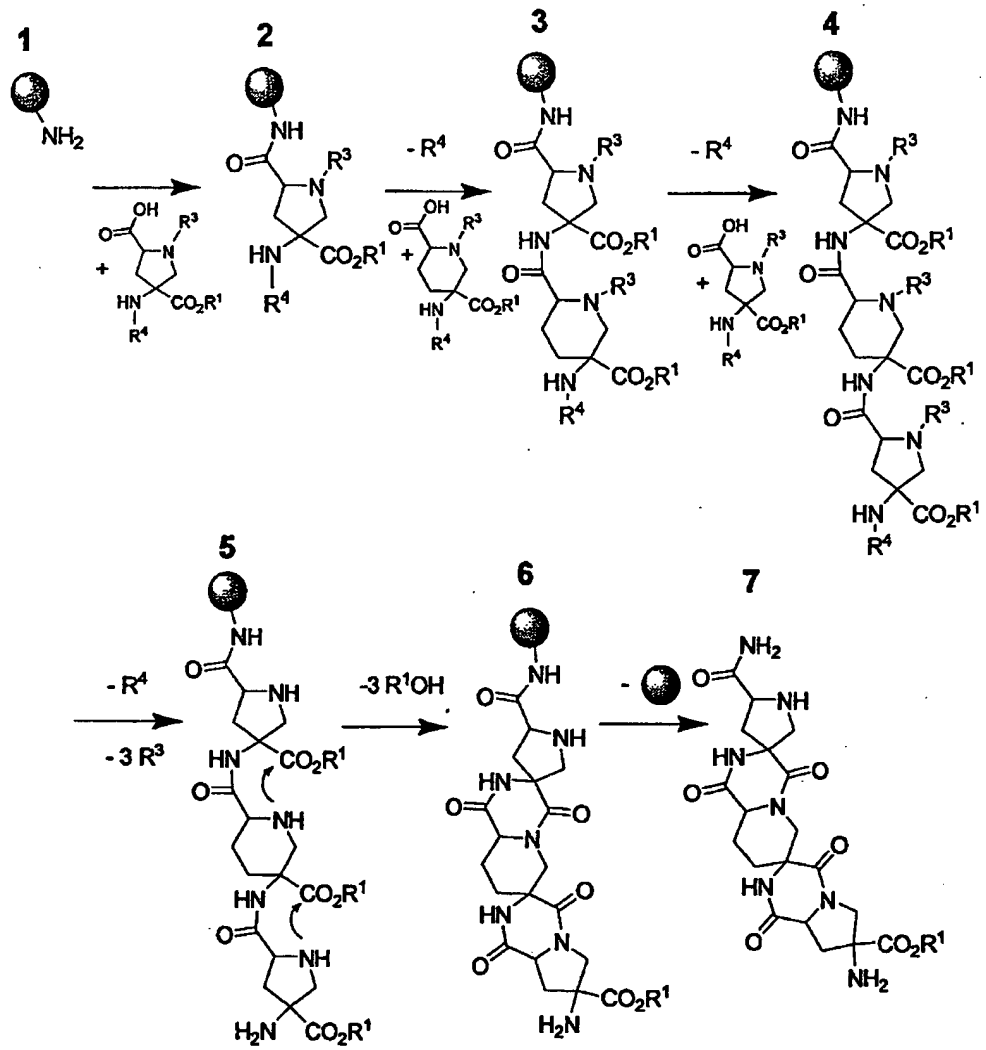

WO9605828
Claim: R1,R2 are both H
or R1, R2 are a carboxyl protecting group

Our patent: Serial No. 10/613,961
Claim: R2 is H
and R1 is a "weak leaving group"
(in other words, R1 is a carboxyl protecting group)

11. That the structure of our building blocks allow assembly of our building blocks to create nanoscale spiro-ladder oligomers for biomimetic and nanotechnology applications using a complex scheme as shown following (steps 1-7) – see paragraph 12.

12. That the function of our building blocks, is to create nanoscale structures. We use one free carboxylic acid to couple a building block to the growing chain (see step 1->2, 2->3, 3->4). We use R4 as an amino-protecting group that we can remove at each stage of the assembly (see step 2->3, 3->4, 4->5). We use R3 as a different amino-protecting group that we can remove from every building block once the chain has been assembled (see step 4->5) and then we use R1 as a "weak leaving group" that can be displaced in the

rigidification step (see step 5->6). By assembling our building blocks using this complex process we assemble our building blocks into the spiro-ladder oligomer in step 7, in which each building block is connected to the next through a pair of amide bonds.




13. I submit that one skilled in the art would recognize that WO9605828 teaches the use of their compounds as drugs, specifically as metabotropic glutamate receptor antagonists and they teach the formulation of their compounds into pharmaceutical compositions containing excipients and the formulation into tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrup, aerosols, and ointments for human consumption. WO9605828 never describes the linking together of their compounds to create nanoscale structures for biomimetic and nanotechnology

applications. Because the intended application of the WO9605828 compounds are as drugs for "use in treating or preventing a physiological condition associated with an inappropriate stimulation of a glutamate receptor in a mammal" (see claim 7, pg 94 WO9605828), one skilled in the art would recognize that they only need compounds that will, in their active form within the body, have two free carboxylic acids as required for binding to the glutamate receptor (page 12 of WO9605828 teaches that the preferred compounds have R1, R2, R4 being H because those are believed to best process antagonist activity at the metabotropic receptors).

14. I submit that one skilled in the art would recognize that U.S. 5,473,077 and WO9605828 describe compounds that are used as drugs. They never describe the linking of their compounds to create oligomers or polymers of any kind. Our compounds are intended to be linked together to create functional nanostructures for nanotechnology and biomimetic applications. Our compounds are never intended by themselves to be used as drugs.

15. Based on my familiarity with the invention, the pending application U.S. Serial No. 10/613,961, the current amendment to which this Declaration will be attached and a review of the applied cited art; it is my considered opinion that the invention as set forth in claims 1-8 and 301-303 viewed with the combination of the applied cited art would in no manner be obvious to one skilled in the art to which the invention pertains.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

6/07/06
Date

Christian E. Schafmeister
Christian E. Schafmeister, Ph.D.

## PUBLICATIONS ATTACHMENT


1. *"Flexibility and Lengths of Bis-peptide Nanostructures by Electron Spin Resonance", Pornsuwan, S., Bird, G., Schafmeister, C. E. and Saxena, S., (2006) *Journal of the American Chemical Society*,128: 3876-3877.
2. *"Molecular chirality and charge transfer through self-assembled scaffold monolayers", Wei, J. J., Schafmeister, C., Bird, G., Paul, A., Naaman, R. and Waldeck, D. H., (2006) *Journal of Physical Chemistry B*,110: 1301-1308.
3. * "Synthesis of curved and linear molecules from a minimal monomer set" Levins, C.G., Schafmeister, C.E. (2005) *J. Org. Chem.*, 70, 9002-9008.
4. * "Synthesis of a pipecolic acid based bis-amino acid and its assembly into a spiro-ladder oligomer" Gupta, S., Das, B.C., Schafmeister, C.E. (2005) *Org. Lett.* 7, 2861-2864
5. * "Synthesis of a Bis-amino Acid that Creates a Sharp Turn" Habay, S.A., Schafmeister, C.E. (2004) *Org. Lett.* 6, 3369-3371
6. * "The Synthesis of Functionalized Nanoscale Molecular Rods of Defined Length" Levins, C.G., Schafmeister C.E. (2003) *J. Am. Chem. Soc.* 125, 4702-4703
7. "An All-Hydrocarbon Cross-Linking System for Enhancing the Helicity and Metabolic Stability of Peptides" Schafmeister, C.E., Po, J., Verdine, G.L., (2000), *J. Am. Chem. Soc.*, 122, 5891-5892
8. "A designed four helix bundle protein with native-like structure", Schafmeister, C.E., LaPorte, S, Miercke, L.J.W., Stroud, R.M., (1997) *Nature Structural Biology*, 4(12), 1039-1046.
9. "Partitioning Roles of Side Chains in Affinity, Orientation, and Catalysis with Structures for Mutant Complexes: Asparagine-229 in Thymidylate Synthase", Finer-Moore, J.S., Liu, L, Schafmeister, C.E., Birdsall, D.L., Mau, T, Santi, D.V., Stroud, R.M., (1996), *Biochemistry*, 35(16), 5125-5136.
10. "Structure at 2.5Å of a Designed Peptide That Maintains Solubility of Membrane Proteins", Schafmeister, C.E., Miercke, L.J.W., Stroud, R.M., (1993), *Science*, 262, 734-738
11. "Fast algorithm for generating CPK images on graphics workstations.", Schafmeister, C., (1990) *J. Mol. Graph.*, 8(4), 201-208